

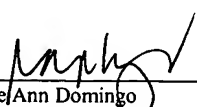


**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**Applicants:** Hebert T. Nagasawa et al. **Examiner:** Not yet known  
**Serial No.:** 10/750,005 **Group Art Unit:** 1646  
**Filed:** December 30, 2003 **Docket No.:** 30451.2USU1  
**Title:** METHODS FOR REDUCING OXIDATIVE STRESS IN A CELL WITH A  
SULFHYDRYL PROTECTED GLUTATHIONE PRODRUG

**CERTIFICATE UNDER 37 CFR §1.8:**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on February 28, 2005.

By:   
Richelle Ann Domingo

**INFORMATION DISCLOSURE STATEMENT**  
**(37 C.F.R. § 1.97(b)(3))**

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Dear Sir:

This statement should be considered because it is submitted before the mailing date of the first Office Action on the merits according to 37 C.F.R. §1.97(b)(3). In accordance with 37 C.F.R. §1.98(d), copies of Exhibits 20-27 as set forth in the Form 1449 are included herein.

With regard to the above-identified application, the items of information listed on the enclosed Form 1449 are brought to the attention of the Examiner. They are as follows:

- Cranskshaw, Duane L. et al., "Double-Prodrugs of L-Cysteine: Differential Protection Against Acetaminophen-Induced Hepatotoxicity in Mice," *Journal of Biochemical and Molecular Toxicology*, November 5, 2002, 16:235-44. – **Exhibit 20**

- Deneke, Susan M. and Barry L. Fanburg, "Regulation of Cellular Glutathione," *American Journal of Physiology*, October 1989, 257(4):L163-73. – **Exhibit 21**
- Dizdar, Nil et al., "Comparison of N-acetylcysteine and L-2-oxothiazolidine-4-carboxylate as Cysteine Deliverers and Glutathione Precursors in Human Malignant Melanoma Transplants in Mice," *Cancer Chemotherapy and Pharmacology*, 2000, 45:192-8. – **Exhibit 22**
- Fernandez-Checa, Jose C. et al., "Mitochondrial Glutathione Depletion in Alcoholic Liver Disease," *Alcohol*, 1993, 10(6):469-75. – **Exhibit 23**
- Holleschau, Ann M. et al., "An HPLC Radiotracer Method for Assessing the Ability of L-Cysteine Prodrugs to Maintain Glutathione Levels in the Cultured Rat Lens," *Current Eye Research*, May 1996, 15(5):501-10. – **Exhibit 24**
- Meister, Alton, "Glutathione Deficiency Produced by Inhibition of its Synthesis, and its Reversal; Applications in Research and Therapy," *Pharmacology and Therapeutics*, 1991, 51(2):155-94. – **Exhibit 25**
- Nagasawa, Herbert T. et al., "Protection Against Acetaminophen-Induced Hepatotoxicity by L-CySSME and its N-Acetyl and Ethyl Ester Derivatives," *Journal of Biochemical Toxicology*, November 6, 1996, 11:289-95. – **Exhibit 26**
- Roberts, Jeanette C. et al., "Prodrugs of L-Cysteine as Protective Agents Against Acetaminophen-Induced Hepatotoxicity. 2-(Polyhydroxyalkyl)- and 2-(Polyacetoxyalkyl)thiazolidine-4(R)-carboxylic Acids," *Journal of Medicinal Chemistry*, 1987, 30:1891-6. – **Exhibit 27**

This statement should be considered because it is submitted before the mailing date of the first Office Action on the merits according to 37 C.F.R. §1.97(b)(3). In accordance with 37 C.F.R. §1.98(a)(2), copies of each document or other information listed on the enclosed Form 1449 are provided.

No representation is made that a reference is "prior art" within the meaning of 35 U.S.C. §§ 102 and 103 and Applicants reserve the right, pursuant to 37 C.F.R. § 1.131 or otherwise, to establish that the reference(s) are not "prior art." Moreover, Applicants do not represent that the references have been thoroughly reviewed or that any relevance of any portion of a reference is intended.

Consideration of the items listed is respectfully requested. Applicants invite the Patent Office to request additional information if necessary. Pursuant to the provisions of M.P.E.P. § 609, it is requested that the Examiner return a copy of the attached Form 1449, marked as being considered and initialed by the Examiner, to the undersigned with the next official communication.

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee, or credit any overpayment, to Deposit Account No. 50-0306.

Respectfully submitted,



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<b>FORM 1449*</b> <b>INFORMATION DISCLOSURE STATEMENT</b> <b>FOR A PATENT APPLICATION</b>  (Use several sheets if necessary)	MAR 02 2005 PATENT & TRADEMARK OFFICE	Docket Number 30451.2USU1	Application Number 10/750,005
	Applicant Herbert T. Nagasawa and Jonathan F. Cohen		
	Filing Date December 30, 2003	Group Art Unit 1646	
	OIPE JC37 MAR 02 2005 PATENT & TRADEMARK OFFICE		

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

## FOREIGN PATENT DOCUMENTS

DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
					YES	NO

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Cranskshaw, Duane L. et al., "Double-Prodrugs of L-Cysteine: Differential Protection Against Acetaminophen-Induced Hepatotoxicity in Mice," <i>Journal of Biochemical and Molecular Toxicology</i> , November 5, 2002, 16:235-44. – <b>Exhibit 20</b>
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EXAMINER	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.	

\*Substitute Disclosure Statement Form (PTO-1449)

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FORM 1449\*

**INFORMATION DISCLOSURE STATEMENT  
IN AN APPLICATION**

(Use several sheets if necessary)

Docket Number

30451.2USU1

Application Number

10/750,005

Applicant

Herbert T. Nagasawa and Jonathan F. Cohen

Filing Date

December 30, 2003

Group Art Unit

1646

**U.S. PATENT DOCUMENTS**

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**FOREIGN PATENT DOCUMENTS**

DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
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**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, Etc.)

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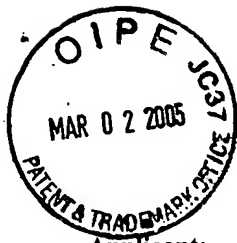
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\*Substitute Disclosure Statement Form (PTO-1449)

Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE



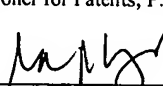
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CERTIFICATE UNDER 37 CFR 1.8

I hereby certify that this paper or fee is being deposited with the United States Postal as first class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on February 28, 2005.

By:   
Name: Richelle Ann Domingo

MAIL STOP AMENDMENT

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Sir:

We are transmitting herewith the attached:

- ☒ Transmittal sheet, in duplicate, containing Certificate under 37 CFR 1.8.
- ☒ Information Disclosure Statement (37 C.F.R. §1.97 (b)(3))
- ☒ Form 1449 (Information Disclosure Statement)
- ☒ Exhibits 20-27
- ☒ Return postcard

Please charge any additional fees or credit overpayment to Deposit Account No. 50-0306. A duplicate of this sheet is enclosed.

MANDEL & ADRIANO

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